CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75405

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS

DIVISION OF BIOEQUIVALENCE

ANDA # 75-405 SPONSOR: Bedford Laboratories.
DRUG AND DOSAGE FORM: Cladribine Injection
Strength(s): 1 mg/ml
Type of Study: SD SDF MULT OTHER
X

STUDY SITE: N/A
STUDY SUMMARY: N/A
FORMULATION: Acceptable
Waiver is granted.

PRIMARY REVIEWER: Mamata S. Gokhale, Ph.D. BRANCH: III
INITIAL MSG DATE 9/24/98

for TEAM LEADER: Barbara M. Davit, Ph.D. BRANCH: III
INITIAL /S/ Date 9/24/98

for DIRECTOR: Dale P. Conner, D.Pharm.
DIVISION OF BIOEQUIVALENCE
INITIAL /S/ DATE 9/24/98

DIRECTOR
OFFICE OF GENERIC DRUGS
INITIAL _____ DATE _____

Cladribine Injection
1 mg/ml, 10 ml vial
ANDA # 75-405
Reviewer: Mamata S. Gokhale

Bedford Laboratories.
Division of Ben Venue Laboratories, Inc.
300 Northfield Road
Bedford, Ohio 44146
Submission Date: June 29, 1998

Review of a Waiver Request

Background

1) The firm has submitted a request for a waiver of in vivo bioavailability/bioequivalance study requirements based on 21 CFR 320.22(b)(1) for its proposed product Cladribine Injection, 1 mg/ml, 10 ml vial. The reference listed product is Leustatin® Injection, supplied in vials as 1 mg/ml (NDA #N20229 001, granted to Johnson RW) manufactured by Ortho Biotech Inc.
2) Cladribine is a synthetic antineoplastic agent indicated for the treatment of acute Hairy Cell Leukemia as defined by clinically significant anemia, neutropenia, thrombocytopenia or disease related symptoms. This purine nucleoside analog exerts cytotoxicity towards dividing as well as quiescent lymphocytes and monocytes by inhibiting both DNA synthesis and repair.
3) The reference product, Leustatin® Injection, 1 mg/ml, is to be administered by the intravenous route (continuous infusion). The test product, Cladribine Injection, 1 mg/ml, is proposed to be administered by similar route.

Formulation Comparison

Comparative compositions of test and reference listed products as specified in the package insert:

Ingredient (per ml)	Reference listed product	Test product
*Cladribine	mg	mg
Sodium Chloride, USP	mg	mg
#Phosphoric Acid, NF	to adjust pH	to adjust pH
#Dibasic Sodium Phosphate Anhydrous, USP	to adjust pH	to adjust pH
	q.s.	q.s.
	-	q.s.

*Active ingredient, #pH range of 5.5-8.0,

Comments

1) The proposed product is a parenteral solution intended for administration solely by injection by the intravenous route.
2) The active ingredient, route of administration, dosage form and strength of the test product are same as those of the reference listed product.
3) All ingredients in test and reference products are qualitatively and quantitatively the same.

Recommendations

The Division of Bioequivalence agrees that the information submitted by Bedford Laboratories demonstrates that Cladribine injection, 1 mg/ml, falls under 21 CFR 320.22(b)(1) of the Bioavailability/Bioequivalence regulations. The waiver of an *in vivo* bioequivalence study requirement for Cladribine injection, 1 mg/ml, is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test product to be bioequivalent to Leustatin® Injection, 1 mg/ml manufactured by Ortho Biotech Inc.

Mamata S. Gokhale, Ph.D. /S/ 9/24/98
Review Branch III
Division of Bioequivalence

for RD INITIALED BDAVIT
FT INITIALED BDAVIT /S/ Date 9/24/98

for Concur: /S/ Date 9/24/98
Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

cc: ANDA# 75-405 (original, duplicate), Gokhale, HFD-658, Drug File, Division File

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA # 75-405 APPLICANT: Bedford Laboratories

DRUG PRODUCT: Cladribine Injection
1 mg/ml

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These Comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research